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Position Statement

Consensus statement on the management of dyslipidaemias in adults☆

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1. Introduction

Most cases of dyslipidaemia increase the risk of ischaemic cardiovascular (CV) complications, while their treatment can reduce CV morbidity and mortality. There is, therefore, a broad international consensus for promoting treatment, although with some variations in approach. As previous French recommendations for dyslipidaemia treatment date back 10 years, they are no longer up to date and have been retracted. However, the complex and evolving differences between the recommendations of European societies (EAS/ESC) [1–3], the International Atherosclerosis Society (IAS) [4], and national bodies in the US (AHA/ACC) [5,6] and Great Britain (NICE) [7] mean that it has become necessary for practitioners to have an updated consensus statement informed by the latest clinical trials.

Thus, a synthesis integrating features from both American and European recommendations was created. A condensed version for the sake of simplicity is presented here, although readers may refer to the primary source documents via the references selected by members of the working group (WG). This consensus statement concerns the general population and does not address either familial hypercholesterolaemia [8–10] or diabetic dyslipidaemia [11,12] in detail. This text is consistent with the opinions of the WG, and has been validated by external readers from three of the societies involved and based on data from the literature available up to 2016.[1]

2. Initial evaluation

2.1. Identification of secondary dyslipidaemia

Secondary dyslipidaemia must be ruled out through investigation of the diseases and treatments that could cause hyperlipidaemia. This involves checking, when appropriate, thyroid-stimulating hormone (TSH), blood glucose, urine protein by dipstick and creatininaemia. Hypothyroidism and cholestasis can induce hypercholesterolaemia; however, the

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[1] Grading the recommendations was done using the HAS scoring system from A to C for decreasing levels of strength, and from 1 to 3 for quality evaluation of the literature on which it is based.

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Table 1
Major cardiovascular risk factors (CVRF) to be considered in subjects with dyslipidaemia.

CVRF
Age (men ≥ 50 years, women ≥ 60 years)
Ischaemic CV family history (men ≤ 55 years, women ≤ 60 years)
Current smoker or quit for < 3 months
Hypertension
HDLc ≤ 0.40 g/L (≤ 1.0 mmol/L)
Type 2 diabetes (or type 1 diabetes for > 15 years and age > 40 years)
Renal failure (GFR < 45 mL/min, < 60 mL/min in young adults)

HDLc: high-density lipoprotein cholesterol; GFR: glomerular filtration rate.

clinical context of cholestasis is generally suggestive. Nephrotic syndromes can cause severe mixed hyperlipidaemia. Diabetes, renal insufficiency and excessive alcohol consumption result in hypertriglyceridaemia. The main treatments that increase low-density lipoprotein cholesterol (LDLc) and, often, triglycerides (TG) are cyclosporin, retinoids, corticosteroids, oral ethinylestradiol, certain antiretrovirals, certain neuroleptics and certain targeted therapies in oncology.

2.2. Estimation of CV risk

CV risk needs to be taken into consideration for adjusting the intensity of primary prevention measures (before the occurrence of atherothrombotic complications). Indeed, the risk/benefit ratio of the treatment and its efficacy (number of persons to be treated to avoid ischaemic complications) depend on the magnitude of the expected benefit. This is based on the level of absolute risk of the individual concerned. Risk-calculation models refer to the multifactorial risk of the general population and not to monogenic primary dyslipidaemias, such as familial hypercholesterolaemia, for which the level of risk is underestimated with general models. Risk-calculation models specific to diabetes patients are also available [13–15].

In practice terms, the WG recommends risk evaluation of the general population based on SCORE tables, which estimate the risk of ischaemic CV death at 10 years [adjusted for low-risk European countries, including France, and taking into account high-density lipoprotein cholesterol (HDLc)] [16]. When such tables are not available, the WG suggests pragmatic tallying of the standard cardiovascular risk factors (CVRF) as a substitution method (low CV risk: 0–1 CVRF; intermediate risk: 2 CVRF; high CV risk: ≥ 3 CVRF).

2.2.1. Risk factors and markers

The main CVRF to be taken into consideration in patients with dyslipidaemia are age and gender, family history of CV disease (first-degree relatives), tobacco use, arterial hypertension, decreases in HDLc, the presence of diabetes and severe to moderate chronic renal failure (CRF), Table 1). These all contribute to risk estimation and treatment decision-making.

2.2.1.1. Lipid tests. Lipid tests are needed at the baseline assessment for estimating the individual level of risk, and then during follow-up to evaluate the efficacy of treatment to ensure adherence, to motivate patients with respect to dietary and lifestyle measures, and to guide potential treatment intensification (A1). It is possible to conduct non-fasting lipid tests when the practitioner finds it necessary to facilitate screening in an elderly person or after an acute coronary syndrome (ACS) [17]. Reliability of the LDLc estimate is all the more affected when there is postprandial hypertriglyceridaemia. Although the role of HDLc as a contributory factor of CV protection has been called into question, its plasma determination provides a powerful marker of CV risk and must therefore be maintained in CV risk assessment (A1) [18].

Table 2
Indications for lipoprotein(a) [Lp(a)] assay.

Intermediate or high ischaemic cardiovascular (CV) risk with
Early personal CV history
Recurrent ischaemic CV complications despite effective treatment with statins
Familial hypercholesterolaemia (heterozygous familial hypercholesterolaemia)
Family history of increased Lp(a)

Adapted from Catapano et al. [1], Stone et al. [5] and Nordestgaard [20].

Although no large-scale, double-blind clinical trials have been done with titration of a lipid-lowering treatment to attain an LDLc target, reference markers are necessary for determining the at-risk subject's condition at inclusion and with treatment in relation to levels observed in CV prevention trials (C3). Cholesterol measurements unrelated to HDL [total cholesterol (TC) – HDLc] may be used in the event of hypertriglyceridaemia (HTG). This takes remnants into account and does not require LDLc assay; its value is 0.3 g/L (0.77 mmol/L) above the usual reference values used for LDLc (B2) [19]. Assay of apolipoprotein B (ApoB) plasma concentration does not provide major advantages for estimates of CV risk (B2). Its main clinical relevance is limited to the aetiological diagnosis of mixed hyperlipidaemia to differentiate familial combined hyperlipidaemia from dysbetalipoproteinaemia, in which ApoB is not increased.

Measurement of lipoprotein (a) [Lp(a)], a risk cofactor for familial hypercholesterolaemia and unexplained atherothrombotic states, should not be done systematically, as its assay indications are restricted (B3) (Table 2) [20].

2.2.1.2. Limitations and benefits of other risk markers. The benefits of employing other risk marker assays for clarifying the risk of subjects with dyslipidaemia remain a matter of debate.

2.2.1.2.1. Biological markers. Plasma concentration assays of fibrinogen, ultrasensitive C-reactive protein (us-CRP) [21], homocysteine (excluding unexplained atherothrombotic complications), lipoprotein-associated phospholipase A2 (Lp-PLA2) [22], lipoparticles (such as LpA1), and the identification of small dense LDL and microalbuminuria (apart from diabetes or hypertension) provide no adequate additional predictive value in dyslipidaemic patients.

2.2.1.2.2. Genotyping. In primary (genetic) hyperlipidaemia, genotyping patients at specialized expert centres enables characterization of the relevant disease (investigation of genetic variants of, for example, LDLR, APOB, PCSK9, APOE